

PATENT COOPERATION TREATY

PCT

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01. März 2006

INTERNATIONAL SEARCH REPORT

Vorfrist:

WV:

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|---|
| Applicant's or agent's file reference C62387PC BÖ/sm1 | FOR FURTHER ACTION | |
| | see Form PCT/ISA/220 as well as, where applicable, item 5 below. | |
| International application No. PCT/EP2005/003888 | International filing date (day/month/year) 13/04/2005 | (Earliest) Priority Date (day/month/year) 14/04/2004 |
| Applicant F. HOFFMANN-LA ROCHE AG | | |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 08 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of:

the international application in the language in which it was filed
 a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. Certain claims were found unsearchable (See Box No. II)

3. Unity of invention is lacking (see Box No III)

4. With regard to the title,

the text is approved as submitted by the applicant
 the text has been established by this Authority to read as follows:

5. With regard to the abstract,

the text is approved as submitted by the applicant
 the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

as suggested by the applicant
 as selected by this Authority, because the applicant failed to suggest a figure
 as selected by this Authority, because this figure better characterizes the invention

b. none of the figures is to be published with the abstract

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2005/003888

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material
 - on paper
 - in electronic form
 - c. time of filing/furnishing
 - contained in the international application as filed
 - filed together with the international application in electronic form
 - furnished subsequently to this Authority for the purpose of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2005/003888

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-18

Expression system comprising one or several nucleic acids that comprise
a) at least one nucleic acid for a IL-15/Fc fusion protein
b) at least one promoter
and
c) at least one nucleic acid for a CD5 leader

2. claims: 19, 20

Use of a CD5 leader for the expression of a protein in CHO cells and their derivatives, in particular CHO-K1 cells.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/003888

| A. CLASSIFICATION OF SUBJECT MATTER C07K14/54 C12N15/11 | | | | | | | | | | |
|---|--|-----------------------------|--|-----------------------|---|--|-----------------------------|-----|-----|-----|
| According to International Patent Classification (IPC) or to both national classification and IPC | | | | | | | | | | |
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12N C07K | | | | | | | | | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | | | | | | | | | |
| Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, MEDLINE, EMBASE, BIOSIS, EMBL | | | | | | | | | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left; padding: 2px;">Category*</th> <th style="text-align: left; padding: 2px;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="text-align: left; padding: 2px;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; padding: 2px;">X</td> <td style="padding: 2px;"> YON SU KIM ET AL: "Targeting the IL-15 receptor with an antagonist IL-15 mutant/Fcgamma2a protein blocks delayed-type hypersensitivity" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 160, no. 12, 15 June 1998 (1998-06-15), pages 5742-5748, XP002185136 ISSN: 0022-1767 the whole document </td> <td style="text-align: center; padding: 2px;">1,2,4-7, 12,13, 15,16</td> </tr> <tr> <td style="text-align: center; padding: 2px;">---</td> <td style="text-align: center; padding: 2px;">-/-</td> <td style="text-align: center; padding: 2px;">---</td> </tr> </tbody> </table> | | Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | X | YON SU KIM ET AL: "Targeting the IL-15 receptor with an antagonist IL-15 mutant/Fcgamma2a protein blocks delayed-type hypersensitivity" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 160, no. 12, 15 June 1998 (1998-06-15), pages 5742-5748, XP002185136 ISSN: 0022-1767 the whole document | 1,2,4-7, 12,13, 15,16 | --- | -/- | --- |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | | | | | | | | |
| X | YON SU KIM ET AL: "Targeting the IL-15 receptor with an antagonist IL-15 mutant/Fcgamma2a protein blocks delayed-type hypersensitivity" JOURNAL OF IMMUNOLOGY, THE WILLIAMS AND WILKINS CO. BALTIMORE, US, vol. 160, no. 12, 15 June 1998 (1998-06-15), pages 5742-5748, XP002185136 ISSN: 0022-1767 the whole document | 1,2,4-7, 12,13, 15,16 | | | | | | | | |
| --- | -/- | --- | | | | | | | | |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. | | | | | | | | | | |
| <input checked="" type="checkbox"/> See patent family annex. | | | | | | | | | | |
| * Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed | | | | | | | | | | |
| "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family | | | | | | | | | | |
| Date of the actual completion of the international search 24 January 2006 | | | | | | | | | | |
| Date of mailing of the international search report 28.02.2006 | | | | | | | | | | |
| Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | | | | | | | | | | |
| Authorized officer Strobel, A | | | | | | | | | | |

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/003888

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| A | SUTHERLAND ROBYN M ET AL: "Protective effect of CTLA4Ig secreted by transgenic fetal pancreas allografts" TRANSPLANTATION (BALTIMORE), vol. 69, no. 9, 15 May 2000 (2000-05-15), pages 1806-1812, XP009041013 ISSN: 0041-1337 abstract page 1807, left-hand column, paragraphs 1,4,6 - right-hand column, paragraph 3 ----- | 1-18 |
| A | KIM Y S ET AL: "IMMUNOGLOBULIN-CYTOKINE FUSION MOLECULES: THE NEW GENERATION OF IMMUNOMODULATING AGENTS" TRANSPLANTATION PROCEEDINGS, ORLANDO, FL, US, vol. 30, no. 8, 1998, pages 4031-4036, XP001031432 ISSN: 0041-1345 page 4035, left-hand column, paragraph 3 - right-hand column, paragraph 2; tables 2,3 ----- | 1-18 |
| A | WO 01/57242 A (AURORA BIOSCIENCES CORP ; CUBITT ANDREW B (US); POLLOK BRIAN A (US); S) 9 August 2001 (2001-08-09) page 148 - page 149; example 10; sequence 53 ----- | 9,11-18 |
| A | WO 02/38766 A (ZYMOGENETICS INC) 16 May 2002 (2002-05-16) sequence 17 ----- | 9,11-18 |
| A | WO 03/087320 A (MOLL THOMAS ; STROM TERRY B (US); ZHENG XIN XIAO (US); BETH ISRAEL HOS) 23 October 2003 (2003-10-23) page 33, line 25 - page 34, line 10; sequence 13 ----- | 1-18 |
| E | EP 1 554 307 A (F. HOFFMANN-LA ROCHE AG) 20 July 2005 (2005-07-20) the whole document ----- | 1-18 |
| P, X | FERRARI-LACRAZ SYLVIE ET AL: "Targeting IL-15 receptor-bearing cells with an antagonist mutant IL-15/Fc protein prevents disease development and progression in murine collagen-induced arthritis" JOURNAL OF IMMUNOLOGY, vol. 173, no. 9, 1 November 2004 (2004-11-01), pages 5818-5826, XP002345721 ISSN: 0022-1767 the whole document ----- | 1-18 |
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/003888

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X | US 5 977 318 A (LINSLEY ET AL) 2 November 1999 (1999-11-02) column 7, line 18 – line 35 column 10, line 44 – line 55 ----- | 19,20 |
| X | US 5 977 307 A (FRIDEN ET AL) 2 November 1999 (1999-11-02) column 20, line 64 – column 21, line 22; figure 8 ----- | 19,20 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2005/003888

| Patent document cited in search report | | Publication date | | Patent family member(s) | | Publication date |
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| WO 0157242 | A | 09-08-2001 | AU CA EP JP | 3485301 A 2400013 A1 1255853 A2 2003534775 T | | 14-08-2001 09-08-2001 13-11-2002 25-11-2003 |
| WO 0238766 | A | 16-05-2002 | AU CA EP JP | 3065902 A 2428242 A1 1407017 A2 2004516826 T | | 21-05-2002 16-05-2002 14-04-2004 10-06-2004 |
| WO 03087320 | A | 23-10-2003 | AU | 2003230834 A1 | | 27-10-2003 |
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| US 5977307 | A | 02-11-1999 | | NONE | | |